Appendix A

Changes to the Specification

The paragraph starting at page 1, line 5 is amended as follows:

--TECHNICAL FIELD

This invention relates to a method for assessing predisposition to various conditions based upon polymorphisms in a bone sialoprotein gene, a matrix gla protein gene, an osteopontin gene and/or an osteoprotegerin (OPG)/osteoclastogenesis inhibitory factor (OCIF) gene. More specifically, the invention relates to a method of assessing an individual's predisposition to various pathological calcification conditions including osteoporosis and atherosclerosis by screening for these polymorphisms. The method of the present invention is especially useful in determining allelic variations in the human bone sialoprotein gene, the human matrix gla protein gene, the human osteopontin gene and/or the osteoprotegerin (OPG) /osteoclastogenesis inhibitory factor (OCIF) gene thus predicting predisposition to high or low bone mineral density (BMD). The invention also relates to bone sialoprotein (BSP) genes, matrix gla protein (MGP) genes, ostepeopontin (OPN) genes and OPG/OCIF genes containing the polymorphisms and to probes and primers therefor.--

The paragraph starting at page 5, line 16 is amended as follows:

--SUMMARY OF THE INVENTION

The present invention now provides a method of assessing an individual's predisposition to a selected calcification condition status, which method comprises determining the genotype of the promoter of the bone sialoprotein gene, the promoter of the matrix gla protein gene, the promoter of the osteopontin gene, or the promoter of the OPG/OCIF gene or all four or any combination of two or more out of the four promoters.--

The paragraph starting at page 17, line 6 is amended as follows:

--BRIEF DESCRIPTION OF THE DRAWINGS

In order that the nature of the present invention be more clearly understood, there now follows an example in which reference is made to the Figures shown in the accompanying drawings in which: --

The paragraph starting at page 22, line 13 is amended as follows:

--DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Example 1 (18 year study)

Methods

Subjects. One hundred thirty three women followed up for 18 years (1977-1995) with respect to BMD, biochemical markers, height, and weight were used in the study. A detailed description of the cohort has been previously published (Jorgensen et al., 1996).--

Appendix B

Changes to the Claims

3. (Amended once) A method as claimed in Claim 1 [or Claim 2], wherein it is determined whether the individual is homozygous or heterozygous for an allelic variation of the promoter of the bone sialoprotein gene, the promoter of the matrix gla protein gene, the promoter of the osteopontin gene or the promoter of the OPG/QCIF gene, or all four or a combination of two or more out of the four promoters.

14. (Amended once) A method as claimed in Claim 1 [any preceding claim], comprising amplifying a relevant portion of the DNA of a said gene promoter of said individual.

23. (Amended once) A method of osteoporosis therapy comprising determining a predisposition as claimed in [any one of Claims 1 to 22] Claim 1, and administering a medicament to the individual to prevent or treat osteoporosis or to delay the onset of osteoporosis if the individual is predisposed to low peak bone mass or to a high rate of loss of bone mass.

24. (Amended once) A method of atherosclerosis therapy comprising determining a predisposition as claimed in [any one of Claims 1 to 22] Claim 1, and administering a medicament to the individual to prevent or treat atherosclerosis or to delay the onset of atherosclerosis if the individual is predisposed to pathological arterial calcification.